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LOGINID:SSPTANXR1625

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TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	JUL 02	LMEDLINE coverage updated
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NEWS 4	JUL 02	CHEMCATS accession numbers revised
NEWS 5	JUL 02	CA/CAplus enhanced with utility model patents from China
NEWS 6	JUL 16	CAplus enhanced with French and German abstracts
NEWS 7	JUL 18	CA/CAplus patent coverage enhanced
NEWS 8	JUL 26	USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS 9	JUL 30	USGENE now available on STN
NEWS 10	AUG 06	CAS REGISTRY enhanced with new experimental property tags
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NEWS 12	AUG 06	FSTA enhanced with new thesaurus edition
NEWS 13	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS 14	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
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NEWS 16	AUG 27	USPATOLD now available on STN
NEWS 17	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS 18	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS 19	SEP 13	FORIS renamed to SOFIS
NEWS 20	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS 21	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS 22	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS 23	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 24	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 16:45:45 ON 17 OCT 2007

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 16:45:57 ON 17 OCT 2007

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 16 OCT 2007 HIGHEST RN 950817-67-1
DICTIONARY FILE UPDATES: 16 OCT 2007 HIGHEST RN 950817-67-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

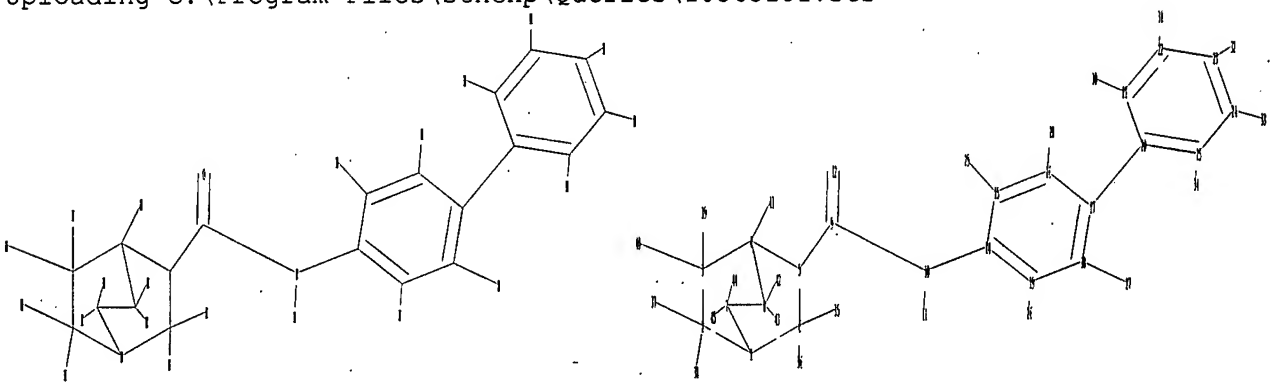
TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10565181.str



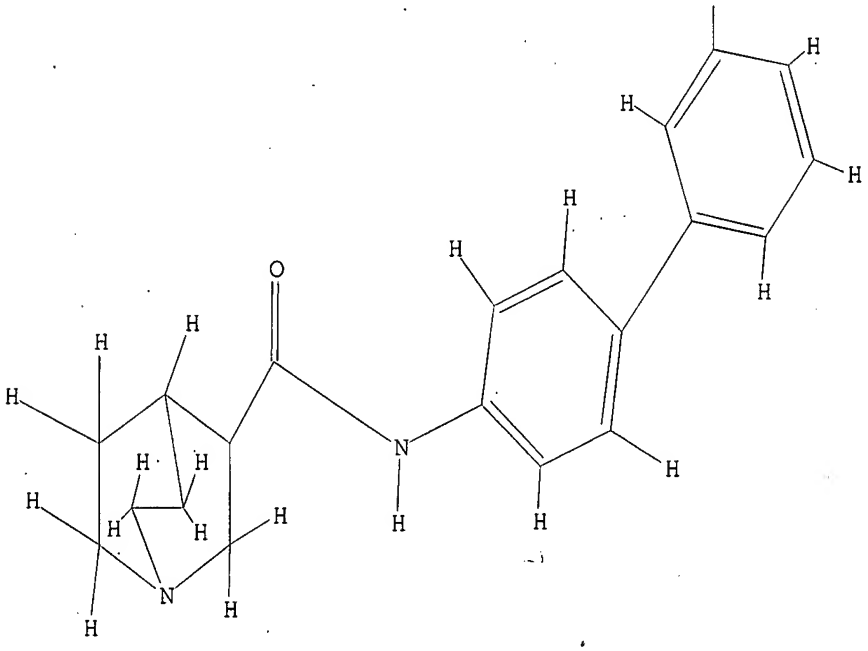
chain nodes :
9 10 11 12 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45
ring nodes :
1 2 3 4 5 6 7 8 14 15 16 17 18 19 20 21 22 23 24 25
chain bonds :
2-37 2-38 3-39 3-40 4-41 5-9 6-35 6-36 7-44 7-45 8-42 8-43 9-10 9-12 10-11 10-14 15-29 16-28 17-20 18-27 19-26 21-30 22-31 23-32 24-33 25-34

ring bonds :
1-2 1-6 1-7 2-3 3-4 4-5 4-8 5-6 7-8 14-15 14-19 15-16 16-17 17-18
18-19 20-21 20-25 21-22 22-23 23-24 24-25
exact/norm bonds :
1-2 1-6 1-7 2-3 3-4 4-5 4-8 5-6 7-8 9-10 9-12 10-14
exact bonds :
2-37 2-38 3-39 3-40 4-41 5-9 6-35 6-36 7-44 7-45 8-42 8-43 10-11 15-29
16-28 17-20 18-27 19-26 21-30 22-31 23-32 24-33 25-34
normalized bonds :
14-15 14-19 15-16 16-17 17-18 18-19 20-21 20-25 21-22 22-23 23-24 24-25
isolated ring systems :
containing 1 : 14 : 20 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:CLASS 10:CLASS
11:CLASS 12:CLASS 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom
21:Atom 22:Atom 23:Atom 24:Atom 25:Atom 26:CLASS 27:CLASS 28:CLASS 29:CLASS
30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS 35:CLASS 36:CLASS 37:CLASS
38:CLASS 39:CLASS 40:CLASS 41:CLASS 42:CLASS 43:CLASS 44:CLASS 45:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1
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SAMPLE SCREEN SEARCH COMPLETED - 7 TO ITERATE

100.0% PROCESSED 7 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

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FULL FILE PROJECTIONS:  ONLINE   **COMPLETE**
                        BATCH    **COMPLETE**
PROJECTED ITERATIONS:             7 TO      298
PROJECTED ANSWERS:                0 TO        0

L2            0 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 16:46:26 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      168 TO ITERATE

100.0% PROCESSED      168 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

L3            0 SEA SSS FUL L1

=> log y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                        ENTRY    SESSION
FULL ESTIMATED COST                                    172.10     172.31

STN INTERNATIONAL LOGOFF AT 16:46:32 ON 17 OCT 2007
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Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTANXR1625

PASSWORD:
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* * * * * * * * * * Welcome to STN International * * * * * * * * * *

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NEWS 2	JUL 02	LMEDLINE coverage updated
NEWS 3	JUL 02	SCISEARCH enhanced with complete author names
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AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
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result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 16:47:33 ON 17 OCT 2007

=> FILE REG

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 16:47:45 ON 17 OCT 2007
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STRUCTURE FILE UPDATES: 16 OCT 2007 HIGHEST RN 950817-67-1
DICTIONARY FILE UPDATES: 16 OCT 2007 HIGHEST RN 950817-67-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

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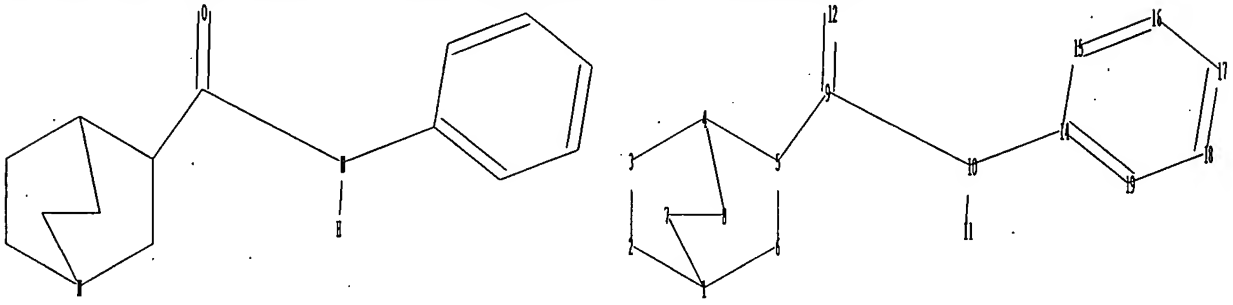

chain nodes :
9 10 11 12
ring nodes :
1 2 3 4 5 6 7 8 14 15 16 17 18 19
chain bonds :
5-9 9-10 9-12 10-11 10-14
ring bonds :
1-2 1-6 1-7 2-3 3-4 4-5 4-8 5-6 7-8 14-15 14-19 15-16 16-17 17-18 18-19
exact/norm bonds :
1-2 1-6 1-7 2-3 3-4 4-5 4-8 5-6 7-8 9-10 9-12 10-14
exact bonds :

5-9 10-11
normalized bonds :
14-15 14-19 15-16 16-17 17-18 18-19
isolated ring systems :
containing 1 : 14 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:CLASS 10:CLASS
11:CLASS 12:CLASS 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom

L1 STRUCTURE UPLOADED

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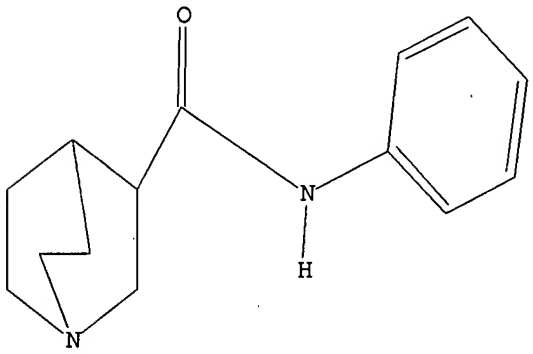
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 16:48:05 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 370 TO ITERATE

100.0% PROCESSED 370 ITERATIONS 3 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS: 6246 TO 8554
PROJECTED ANSWERS: 3 TO 163

L2 3 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 16:48:11 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 7586 TO ITERATE

100.0% PROCESSED 7586 ITERATIONS 80 ANSWERS
SEARCH TIME: 00.00.01

L3 80 SEA SSS FUL L1

=> file caplus'
'CAPLUS'' IS NOT A VALID FILE NAME
SESSION CONTINUES IN FILE 'REGISTRY'

Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files that are available. If you have requested multiple files, you can specify a corrected file name or you can enter "IGNORE" to continue accessing the remaining file names entered.

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	172.10	172.31

FILE 'CAPLUS' ENTERED AT 16:48:20 ON 17 OCT 2007
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 17 Oct 2007 VOL 147 ISS 17
FILE LAST UPDATED: 16 Oct 2007 (20071016/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l3 full
L4 14 L3

=> d ibib abs hitstr tot

L4 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:874444 CAPLUS
DOCUMENT NUMBER: 147:257789
TITLE: 4-Aryl-2-aminopyrimidines or 4-aryl-2-aminoalkylpyrimidines as JAK-2 modulators and their preparation, pharmaceutical compositions and use in the treatment of diseases
INVENTOR(S): Mann, Grace; Aay, Naing; Arcalas, Arlyn; Brown, S. David; Chan, Wai Ki Vicky; Chen, Jeff; Du, Hongwang; Epshteyn, Sergey; Forsyth, Timothy; Galan, Adam A.; Huynh, Tai Phat; Ibrahim, Mohamed Abdulkader; Johnson, Henry William Beecroft; Kane, Brian; Kearney, Patrick; Kim, Byung Gyu; Koltun, Elena; Leahy, James William; Lee, Matthew Sangyup; Lewis, Gary L.; Meyr, Lisa E.; Noguchi, Robin Tammie; Pack, Michael; Ridgway, Brian Hugh; Shi, Xian; Woolfrey, John; Zhou, Peiwen
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 586pp., which which
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007089768	A2	20070809	WO 2007-US2515	20070130
WO 2007089768	A3	20070920		

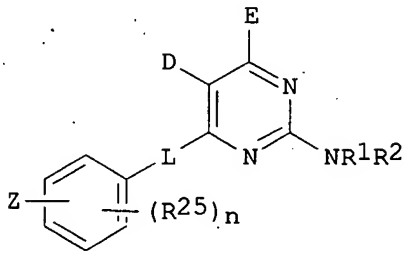
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.:
US 2006-763426P P 20060130
US 2006-785239P P 20060323
US 2006-840420P P 20060825

OTHER SOURCE(S): MARPAT 147:257789

GI



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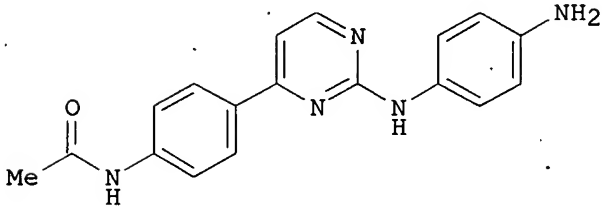


II

AB This invention relates to certain pyrimidine derivative inhibitors of JAK-2, having formula I, pharmaceutically acceptable salts thereof, pharmaceutical compns. thereof, and methods of use thereof. Compds. of formula I wherein D and E are independently H, halo, CF3, heterocycloalkyl and alkyl; DE taken together to form 5- to 7-membered heteroaryl and 5- to 7-membered heterocycloalkyl; L is a bond, O and NH; Z is alkoxyl, cycloalkyl, (un)substituted heteroaryl, aryl, (un)substituted heterocycloalkyl; Z-R25 taken together to form 5- to 6-membered (hetero)cycloalkyl, and 5- to 6-membered heteroaryl; n is 0, 1, 2, 3, and 4; R1 is H; R2 is (un)substituted (hetero)aryl, (un)substituted alkylaryl; R25 is alkyl, alkenyl, halo, haloalkyl, amino, etc.; and their pharmaceutically acceptable salts thereof, are claimed. Example compound II was prepared by cross-coupling of 2,4-dichloropyrimidine with 4-(acetylamino)phenylboronic acid; the resulting N-[4-(2-chloropyrimidin-4-yl)phenyl]acetamide underwent amination with N-Boc-1,3-diaminobenzene to give compound II. All the invention compds. were evaluated for their JAK-2

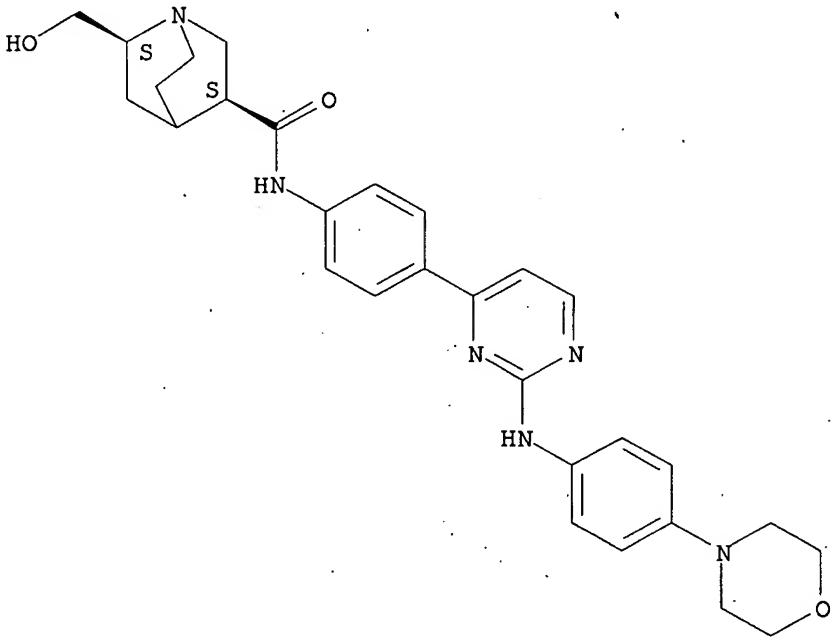
inhibitory activity.

IT 945750-35-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of aryl(amino)pyrimidines and aryl(aminoalkyl)pyrimidines as JAK-2 modulators useful in the treatment of diseases)

RN 945750-35-6 CAPLUS

CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, 6-(hydroxymethyl)-N-[4-[2-[[4-(4-morpholinyl)phenyl]amino]-4-pyrimidinyl]phenyl]-, (3S,6S)- (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:120928 CAPLUS
DOCUMENT NUMBER: 142:198251
TITLE: Preparation of quinuclidine N-biarylamides for use in treatment and/or prophylaxis of diseases
INVENTOR(S): Flessner, Timo; Boess, Frank-Gerhard; Hafner, Frank-Thorsten; Luithle, Joachim; Methfessel, Christoph; Telan, Leila
PATENT ASSIGNEE(S): Bayer Healthcare AG, Germany
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005012299	A1	20050210	WO 2004-EP8037	20040719

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

DE 10334724	A1	20050224	DE 2003-10334724	20030730
CA 2534003	A1	20050210	CA 2004-2534003	20040719
EP 1651645	A1	20060503	EP 2004-741132	20040719
EP 1651645	B1	20070221		
R: DE, ES, FR, GB, IT				
JP 2007500152	T	20070111	JP 2006-521462	20040719
US 2007112023	A1	20070517	US 2006-565181	20061016

PRIORITY APPLN. INFO.: DE 2003-10334724 A 20030730
WO 2004-EP8037 W 20040719

OTHER SOURCE(S): CASREACT 142:198251; MARPAT 142:198251
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

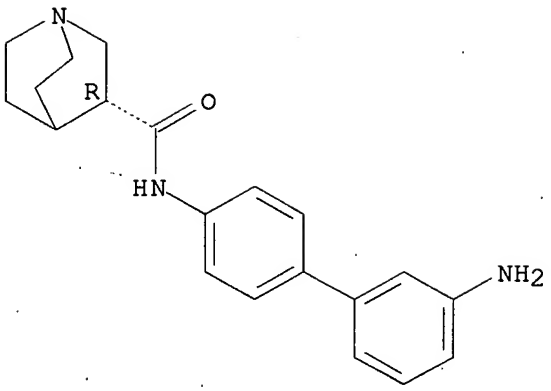
AB The invention relates to N-biarylamides I [R1 = NR2CONR3R4,NR2COCO2R5, NHSO2R6,SO2NHR7, NHCOR8; R2 = H, C1-6-alkyl; R3, R4 = H, C1-6-alkyl, C3-8-cycloalkyl, Ph (optionally substituted with up to three residues from the group halogen, CN, C1-6-alkyl, C1-6-alkoxy, CF3, OCF3); NR3R4 = 5- or 6-membered ring; R5 = H, C1-6-alkyl, C3-8-cycloalkyl, aryl, aryl-(C1-6-alkyl), R6 = C1-6-alkyl, C3-8-cycloalkyl, 5- or 6-membered heterocycle or heteroaryl, aryl-(C1-6-alkyl); R7 = C1-6-alkyl, C3-8-cycloalkyl, aryl, 5- or 6-membered heterocycle or heteroaryl, aryl-(C1-6-alkyl); R8 = C1-6-alkyl, C3-8-cycloalkyl, Ph, Ph-(C1-6-alkyl), (C1-6-alkoxy)-(C1-6-alkyl), (optionally substituted with up to three residues from the group halogen, CN, C1-6-alkyl, C1-6-alkoxy, CF3, OCF3)], their salts, solvates and salt solvates, methods for their production and use thereof for the production of medicaments for the treatment and/or prophylaxis of diseases and for improvement in cognition, concentration power, learning power and/or memory. Procedure for the preparation of I comprises: amidation of quinuclidine II [X = OH, Cl, OC6F5] with amines III or IV [Y = triflate, halogen (especially Br or I)]; with the latter, intermediate V is formed and is coupled with boronic acid VI [R9 = H, Me; (R9)2 = CH2CH2, CMe2CMe2] in an inert solvent containing a catalyst and a base. Thus, I·HCl [R1 = NHSO2Me-4] was prepared from quinuclidin-3-one via deoxidative cyanation, chromatog. resolution, hydrolysis, carbonyl chlorination and amidation with 4-(4-H2NC6H4)C6H4NHSO2Me. The binding ability of I·HCl [R1 = NHSO2Me-4] towards 7α-n acetylcholine receptor was determined [Ki = 2 nM].

IT 838852-86-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acylation, sulfonation or carbamylation of; preparation of quinuclidine N-biarylamides for use in treatment and/or prophylaxis of diseases)

RN 838852-86-1 CAPLUS

CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(3'-amino[1,1'-biphenyl]-4-yl)-, dihydrochloride, (3R)- (9CI) (CA INDEX NAME)

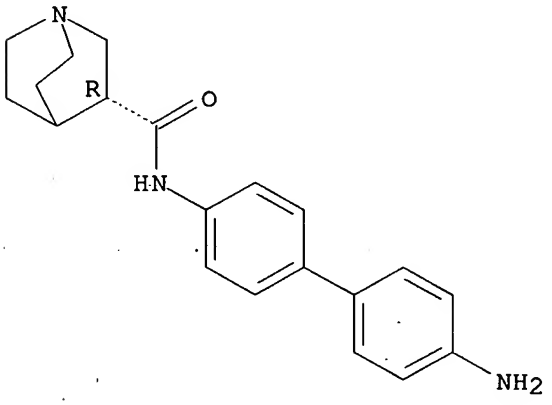
Absolute stereochemistry.



●2 HCl

IT 838852-85-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acylation, sulfonylation or carbamylation of; preparation of
quinuclidine N-biarylamides for use in treatment and/or prophylaxis of diseases)
RN 838852-85-0 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(4'-amino[1,1'-biphenyl]-4-yl)-, dihydrochloride, (3R)- (9CI) (CA INDEX NAME)

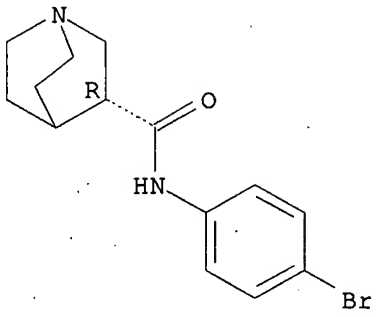
Absolute stereochemistry.



●2 HCl

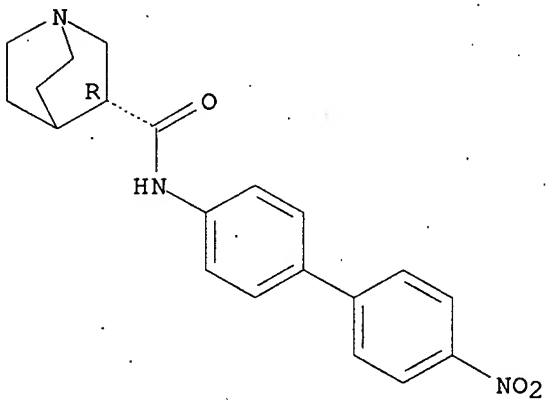
IT 604803-85-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and coupling reactions of, with boronates; preparation of quinuclidine N-biarylamides for use in treatment and/or prophylaxis of diseases)
RN 604803-85-2 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(4-bromophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



IT 838852-84-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenolysis of; preparation of quinuclidine N-biarylamides
for use in treatment and/or prophylaxis of diseases)
RN 838852-84-9 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(4'-nitro[1,1'-biphenyl]-4-yl)-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

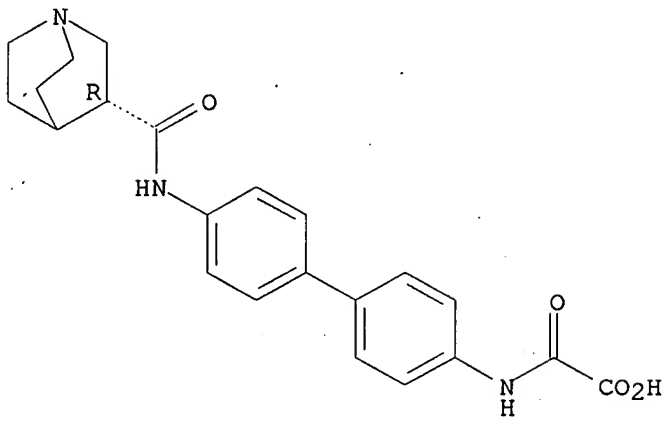
Absolute stereochemistry.



● HCl

IT 838852-67-8P 838852-68-9P 838852-69-0P
838852-70-3P 838852-71-4P 838852-72-5P
838852-73-6P 838852-74-7P 838852-75-8P
838852-76-9P 838852-77-0P 838852-78-1P
838852-79-2P 838852-80-5P 838852-81-6P
838852-82-7P 838852-83-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinuclidine N-biarylamides for use in treatment and/or prophylaxis of diseases)
RN 838852-67-8 CAPLUS
CN Acetic acid, [[4'-[[(3R)-1-azabicyclo[2.2.2]oct-3-ylcarbonyl]amino][1,1'-biphenyl]-4-yl]amino]oxo-, monohydrochloride (9CI) (CA INDEX NAME)

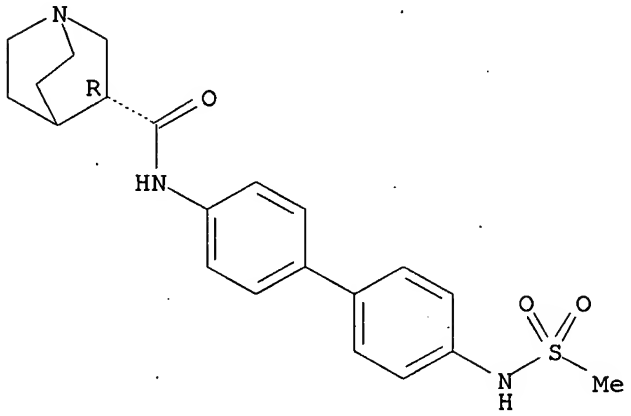
Absolute stereochemistry.



● HCl

RN 838852-68-9 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[(methylsulfonyl)amino][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)-(9CI) (CA INDEX NAME)

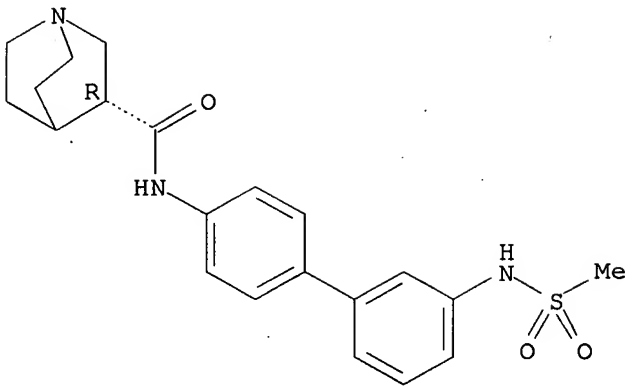
Absolute stereochemistry.



● HCl

RN 838852-69-0 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[3'-[(methylsulfonyl)amino][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)-(9CI) (CA INDEX NAME)

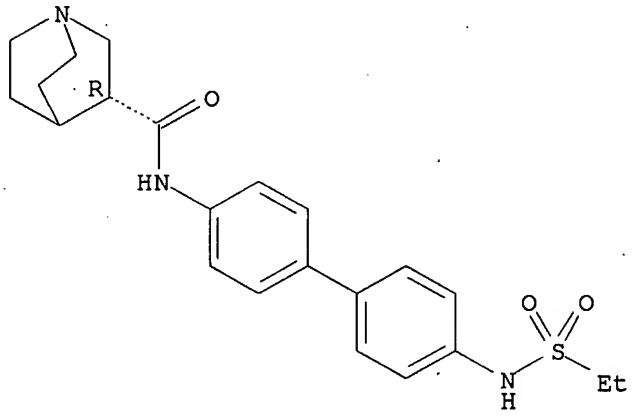
Absolute stereochemistry.



● HCl

RN 838852-70-3 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[(ethylsulfonyl)amino][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

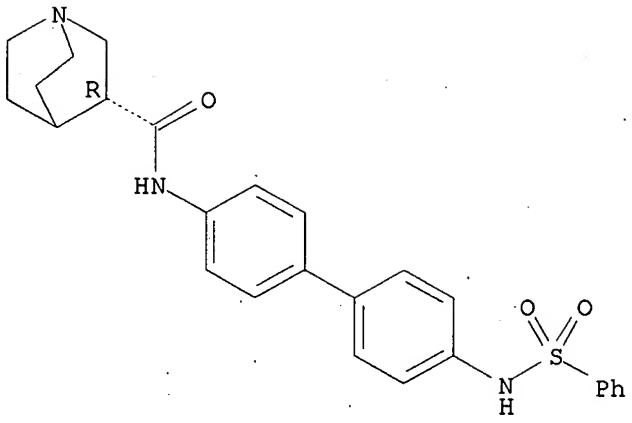
Absolute stereochemistry.



● HCl

RN 838852-71-4 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[(phenylsulfonyl)amino][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

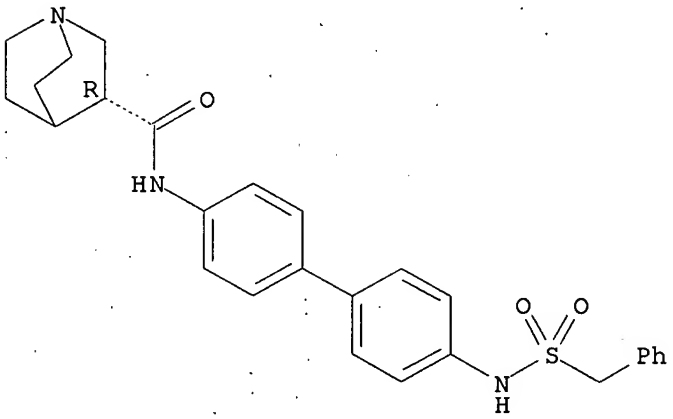
Absolute stereochemistry.



● HCl

RN 838852-72-5 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[[(phenylmethyl)sulfonyl]amino][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

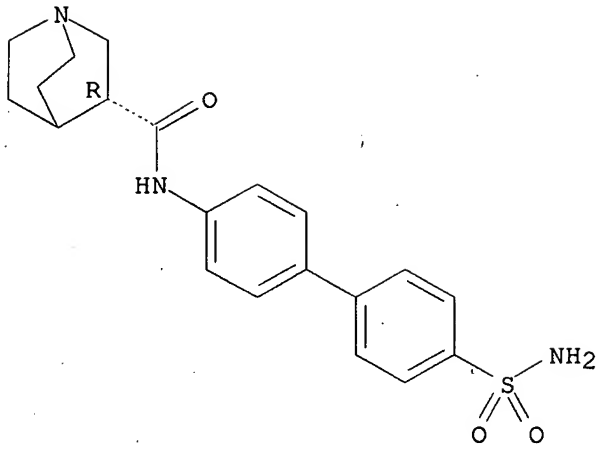
Absolute stereochemistry.



● HCl

RN 838852-73-6 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-(aminosulfonyl)[1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

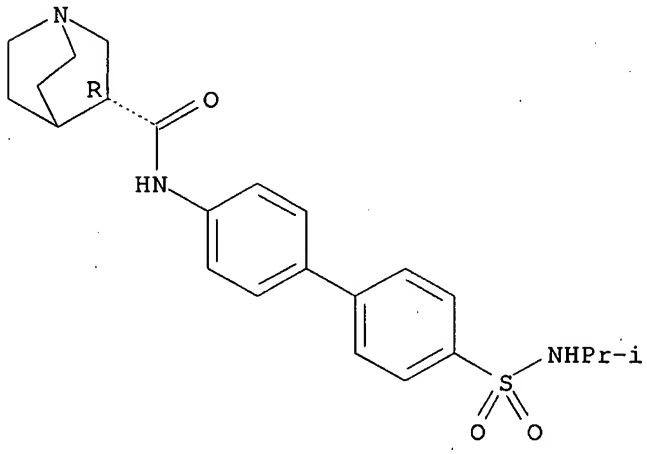
Absolute stereochemistry.



● HCl

RN 838852-74-7 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[[(1-methylethyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

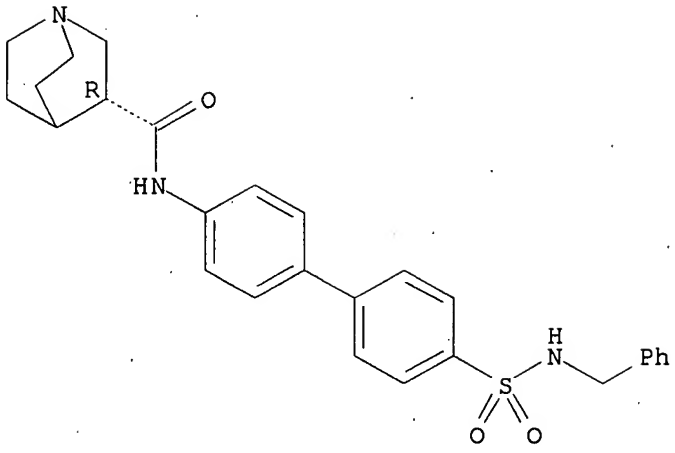
Absolute stereochemistry.



● HCl

RN 838852-75-8 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[[(phenylmethyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

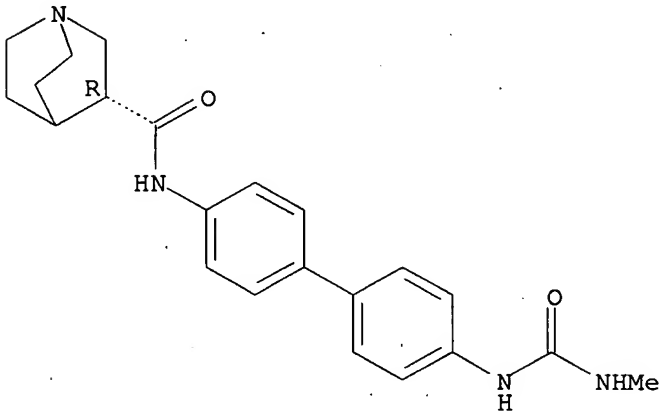
Absolute stereochemistry.



● HCl

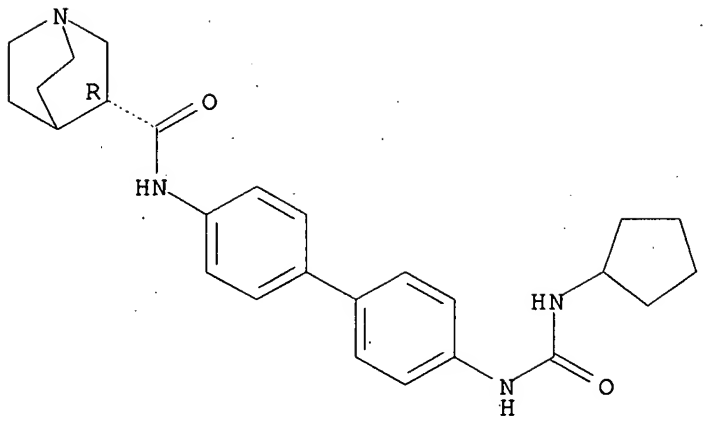
RN 838852-76-9 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[[(methylamino)carbonyl]amino][1,1'-biphenyl]-4-yl]-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RN 838852-77-0 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[[(cyclopentylamino)carbonyl]amino][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

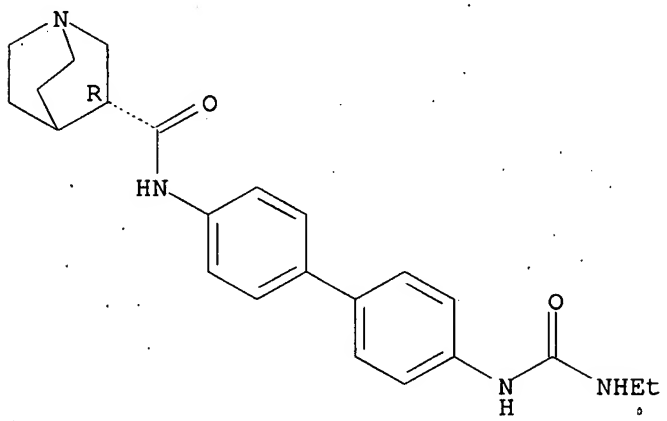
Absolute stereochemistry.



● HCl

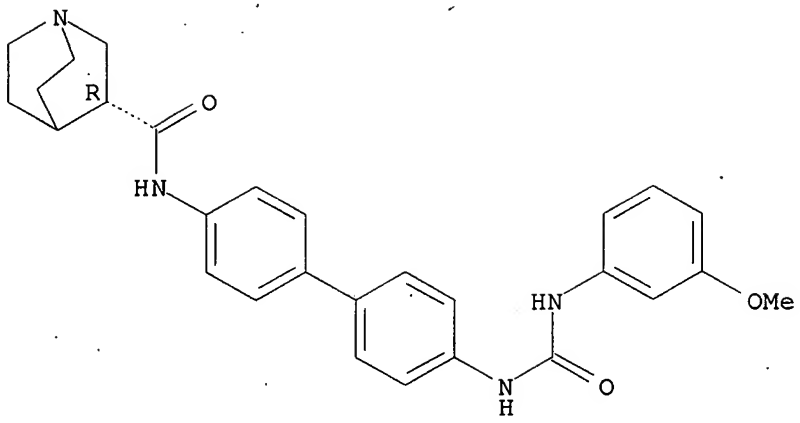
RN 838852-78-1 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[[(ethylamino)carbonyl]amino][1,1'-biphenyl]-4-yl]-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RN 838852-79-2 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[[[(3-methoxyphenyl)amino]carbonyl]amino][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

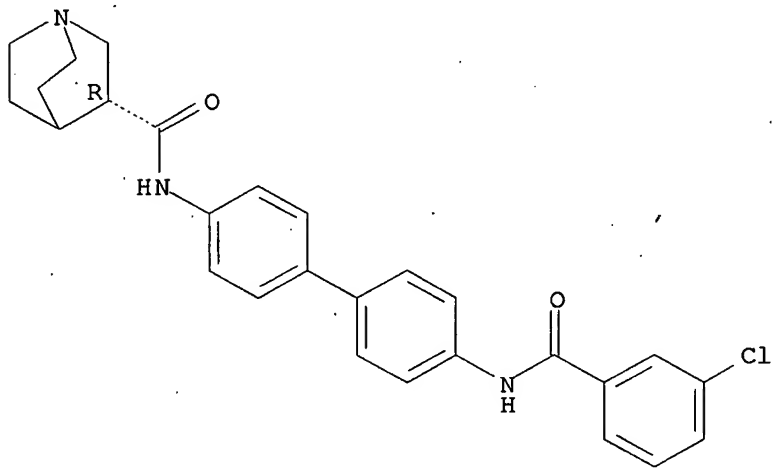
Absolute stereochemistry.



● HCl

RN 838852-80-5 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[(3-chlorobenzoyl)amino][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

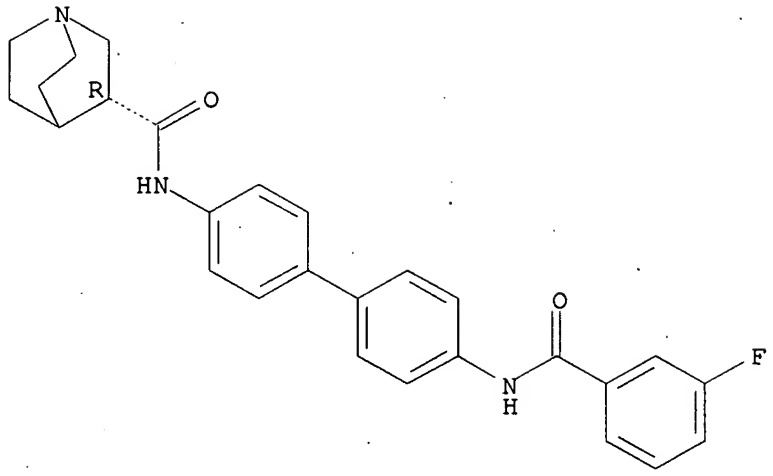
Absolute stereochemistry.



● HCl

RN 838852-81-6 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[(3-fluorobenzoyl)amino][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

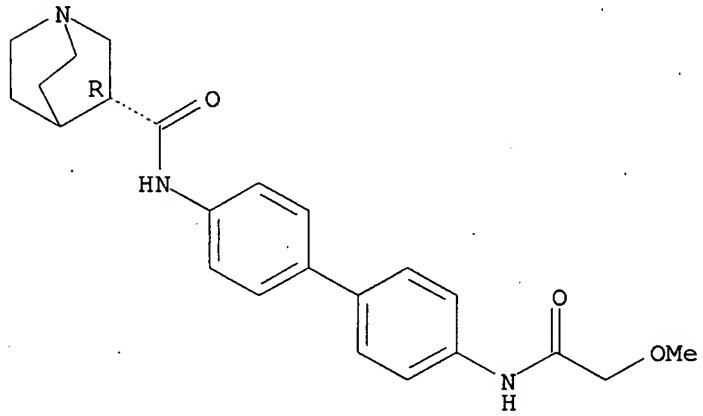
Absolute stereochemistry.



● HCl

RN 838852-82-7 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[(methoxyacetyl)amino][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

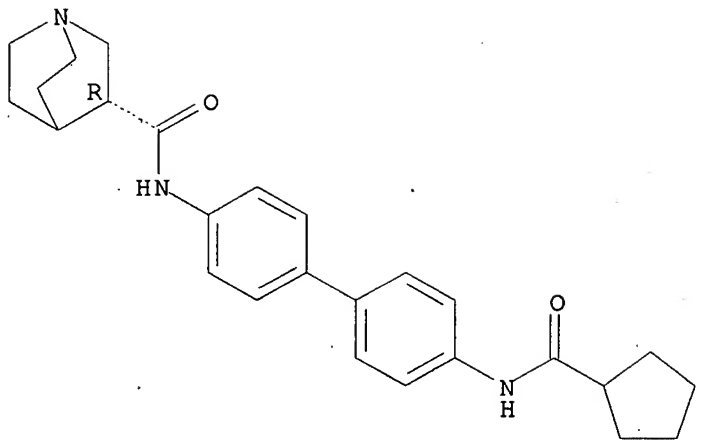
Absolute stereochemistry.



● HCl

RN 838852-83-8 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[(cyclopentylcarbonyl)amino][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:757707 CAPLUS
DOCUMENT NUMBER: 139:277050
TITLE: Preparation of aza-bicyclic N-biarylamides with affinity for the α7-nicotinic acetylcholine receptor
INVENTOR(S): Luithle, Joachim; Boess, Frank-Gerhard; Erb, Christina; Schnizler, Katrin; Flessner, Timo; Van Kampen, Marja; Methfessel, Christoph; Hafner, Frank-Thorsten
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003078431	A1	20030925	WO 2003-EP2153	20030303
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10211415	A1	20030925	DE 2002-10211415	20020315
CA 2479103	A1	20030925	CA 2003-2479103	20030303
AU 2003212296	A1	20030929	AU 2003-212296	20030303
EP 1487834	A1	20041222	EP 2003-708168	20030303
EP 1487834	B1	20070425		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

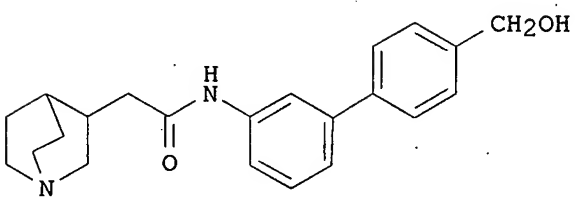
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

JP 2005524675	T	20050818	JP 2003-576436	20030303
US 2005154045	A1	20050714	US 2005-508108	20050303
US 7138410	B2	20061121		

PRIORITY APPLN. INFO.: DE 2002-10211415 A 20020315
WO 2003-EP2153 W 20030303

OTHER SOURCE(S): MARPAT 139:277050

GI



I

AB The azabicyclic N-arylamides, R1AC(:O)NR3ER3 [R1 = 1-azabicyclo[m.n.p]alkyl (7 - 11 ring atoms, optionally substituted with C1-6-alkyl); m, n = 2, 3; p = 1, 2, 3; A = CH2, CH2CH2, propylene; E = 5-6 membered heteroaryl of benzenediyl optionally substituted with halo, cyano, F3C, F3CO, C1-6-alkyl; R2 = 5-6 membered heteroaryl, Ph, optionally substituted with halo, heterocyclyl, carbamoyl, carboxylate, amino, acyl, CN, CF3, CF3O, NO2, C1-6-alkyl, C1-6-alkoxy, C1-6-alkylthio, etc.; R3 = H, C1-6-alkyl] and their salts, solvates and salt solvates were prepared and used for producing pharmaceuticals for the treatment and/or prophylaxis of diseases and for improving perception, concentration, learning ability and memory. Thus, 2-(1-azabicyclo[2.2.2]octan-3-yl)-N-(3-bromophenyl)acetamide hydrochloride was treated with 4-(hydroxymethyl)phenylboronic acid to give the quinuclidineacetamide derivative I. The affinity of I for α7-nAChR was determined

IT 604803-22-7P 604803-23-8P 604803-24-9P
604803-25-0P 604803-34-1P 604803-35-2P
604803-36-3P 604803-37-4P 604803-38-5P
604803-39-6P 604803-40-9P 604803-41-0P
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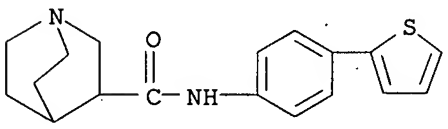
604803-47-6P 604803-49-8P 604803-97-6P
604804-00-4P 604804-02-6P 604804-04-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aza-bicyclic N-biarylamides with affinity for α-7 nicotinic acetylcholine receptor)

RN 604803-22-7 CAPLUS

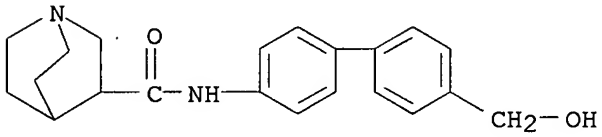
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4-(2-thienyl)phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

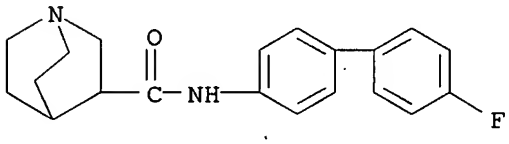
RN 604803-23-8 CAPLUS

CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-(hydroxymethyl)[1,1'-biphenyl]-4-yl]-, monohydrochloride (9CI) (CA INDEX NAME)



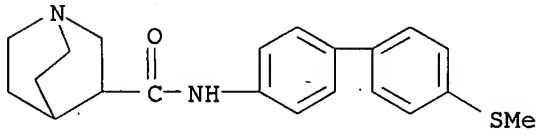
● HCl

RN 604803-24-9 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(4'-fluoro[1,1'-biphenyl]-4-yl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

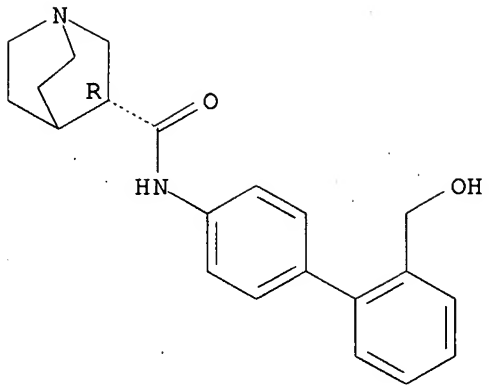
RN 604803-25-0 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-(methylthio)[1,1'-biphenyl]-4-yl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

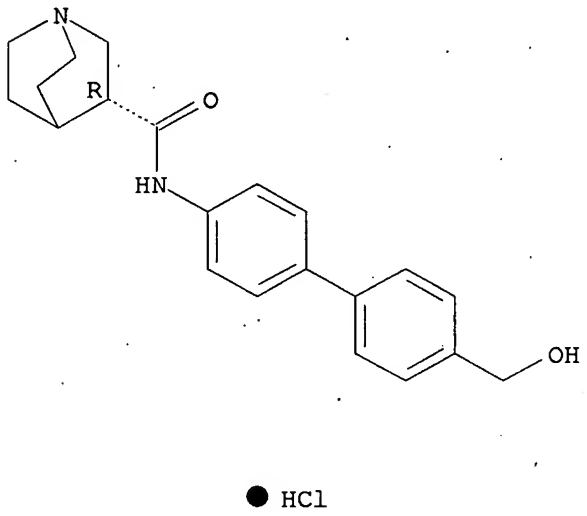
RN 604803-34-1 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[2'-(hydroxymethyl)[1,1'-biphenyl]-4-yl]-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RN 604803-35-2 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-(hydroxymethyl)[1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

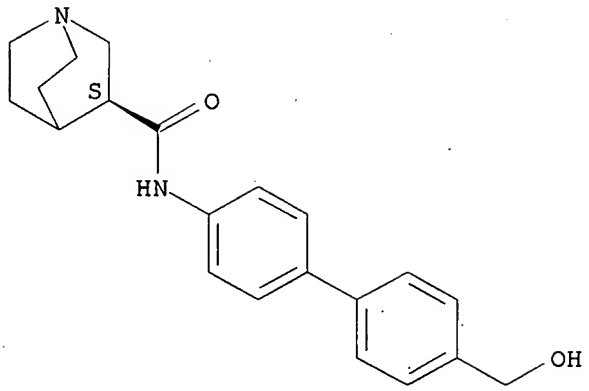
Absolute stereochemistry.



● HCl

RN 604803-36-3 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-(hydroxymethyl)[1,1'-biphenyl]-4-yl]-, monohydrochloride, (3S)- (9CI) (CA INDEX NAME)

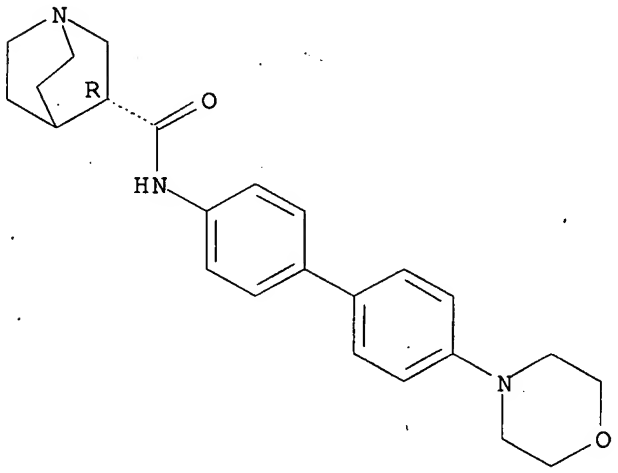
Absolute stereochemistry.



● HCl

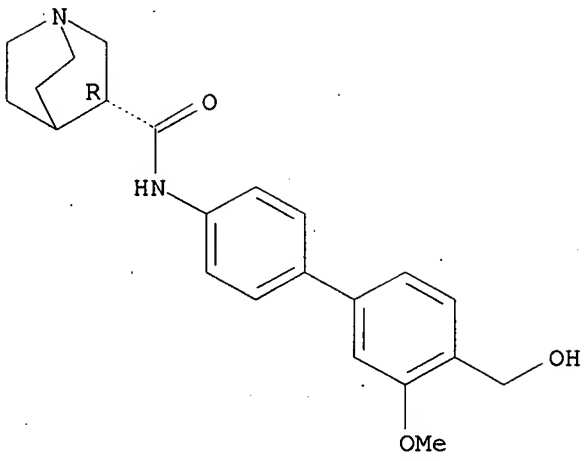
RN 604803-37-4 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-(4-morpholinyl)[1,1'-biphenyl]-4-yl]-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



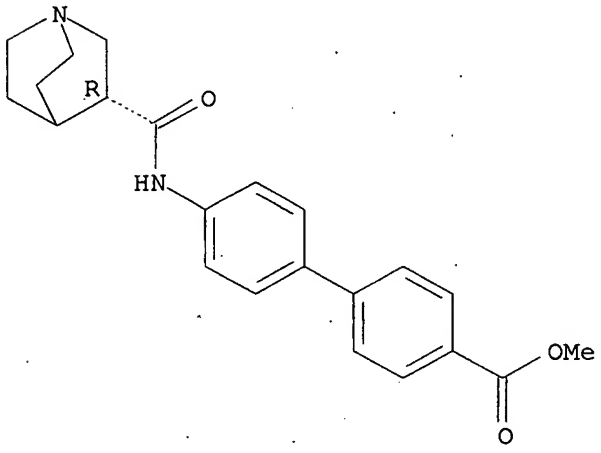
RN 604803-38-5 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-(hydroxymethyl)-3'-methoxy[1,1'-biphenyl]-4-yl]-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



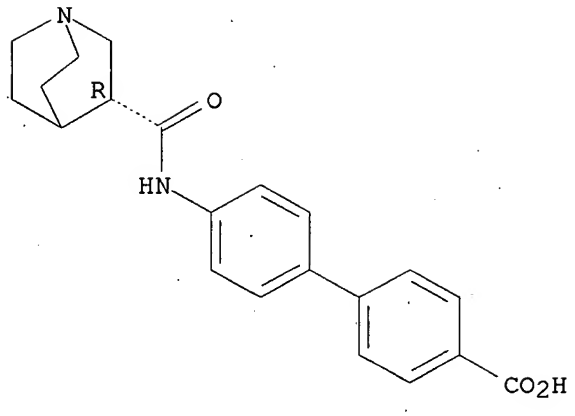
RN 604803-39-6 CAPLUS
CN [1,1'-Biphenyl]-4-carboxylic acid, 4'-[[(3R)-1-azabicyclo[2.2.2]oct-3-ylcarbonyl]amino]-, methyl ester (CA INDEX NAME)

Absolute stereochemistry.



RN 604803-40-9 CAPLUS
CN [1,1'-Biphenyl]-4-carboxylic acid, 4'-[[(3R)-1-azabicyclo[2.2.2]oct-3-ylcarbonyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

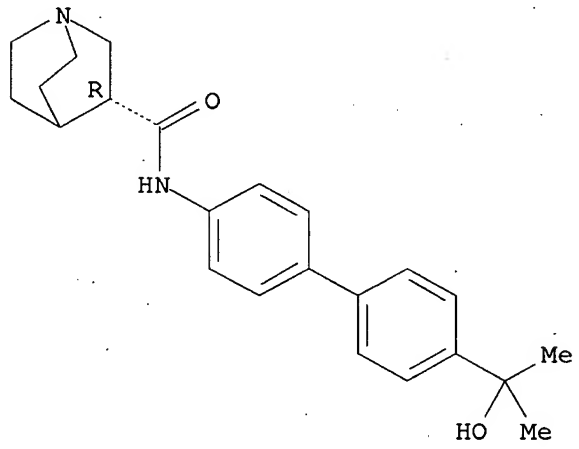
Absolute stereochemistry.



● HCl

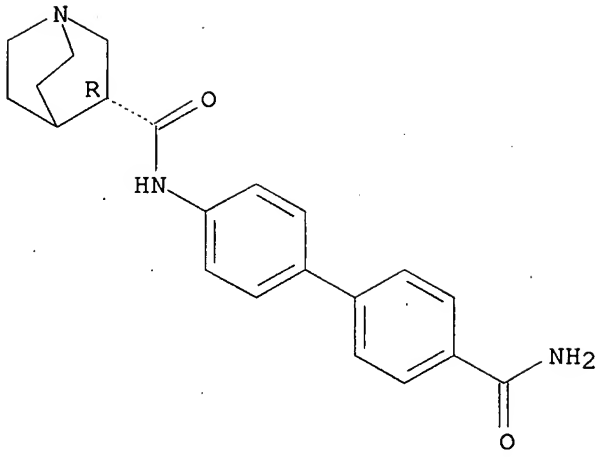
RN 604803-41-0 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-(1-hydroxy-1-methylethyl)[1,1'-biphenyl]-4-yl]-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RN 604803-42-1 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-(aminocarbonyl)[1,1'-biphenyl]-4-yl]-, hydrochloride, (3R)- (9CI) (CA INDEX NAME)

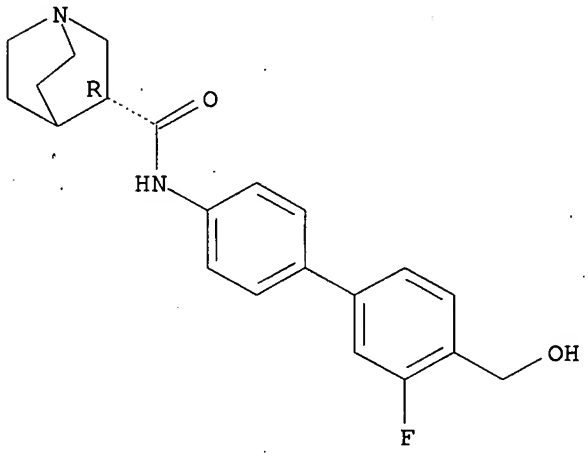
Absolute stereochemistry.



● x HCl

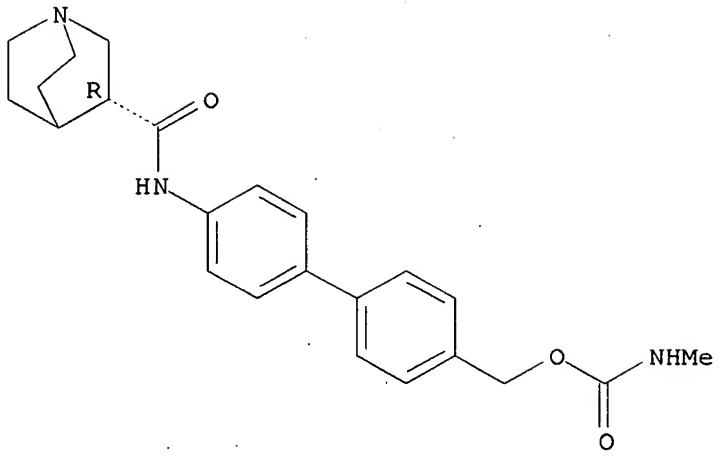
RN 604803-44-3 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[3'-fluoro-4'-(hydroxymethyl)[1,1'-biphenyl]-4-yl]-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



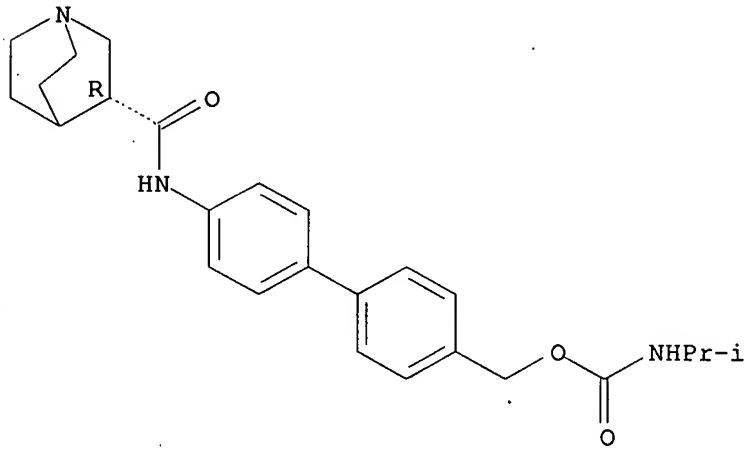
RN 604803-45-4 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[[[(methylamino)carbonyl]oxy]methyl][1,1'-biphenyl]-4-yl]-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



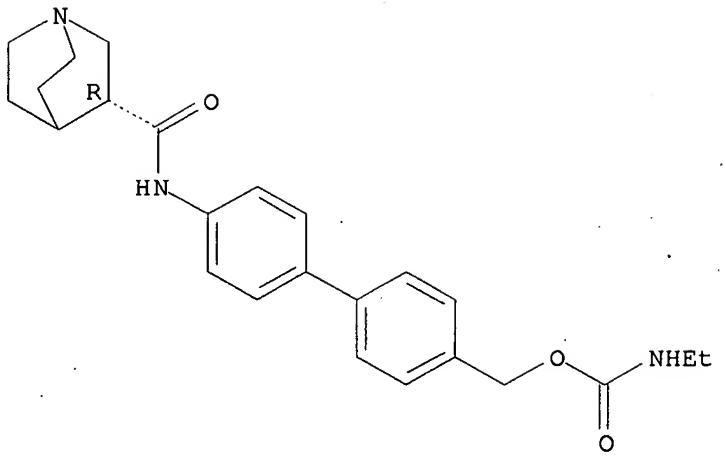
RN 604803-47-6 CAPLUS
CN Carbamic acid, (1-methylethyl)-, [4'-[[(3R)-1-azabicyclo[2.2.2]oct-3-ylcarbonyl]amino][1,1'-biphenyl]-4-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

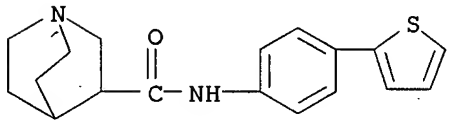


RN 604803-49-8 CAPLUS
CN Carbamic acid, ethyl-, [4'-[[(3R)-1-azabicyclo[2.2.2]oct-3-ylcarbonyl]amino][1,1'-biphenyl]-4-yl]methyl ester (9CI) (CA INDEX NAME)

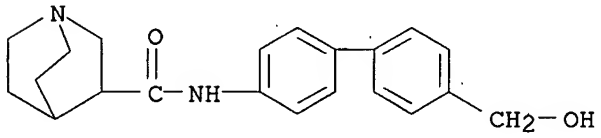
Absolute stereochemistry.



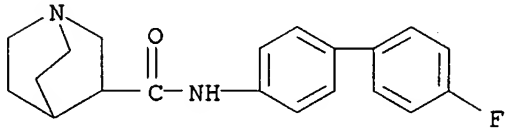
RN 604803-97-6 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4-(2-thienyl)phenyl]- (CA INDEX NAME)



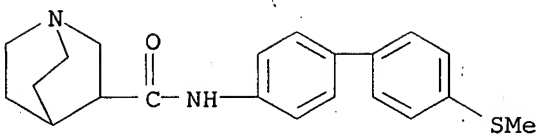
RN 604804-00-4 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-(hydroxymethyl)[1,1'-biphenyl]-4-yl]- (CA INDEX NAME)



RN 604804-02-6 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(4'-fluoro[1,1'-biphenyl]-4-yl)- (CA INDEX NAME)

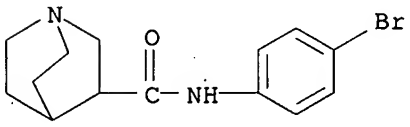


RN 604804-04-8 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-(methylthio)[1,1'-biphenyl]-4-yl]- (CA INDEX NAME)



IT 604803-72-7P 604803-83-0P 604803-85-2P
604804-18-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aza-bicyclic N-biarylamides with affinity for α-7 nicotinic acetylcholine receptor)

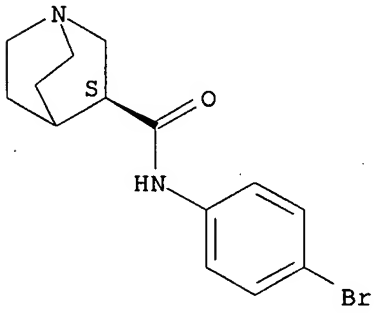
RN 604803-72-7 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(4-bromophenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

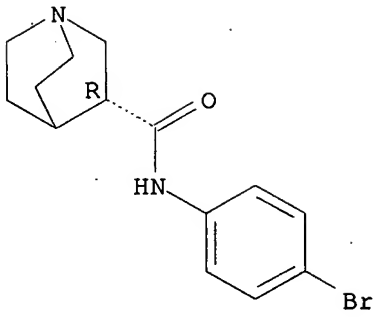
RN 604803-83-0 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(4-bromophenyl)-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.

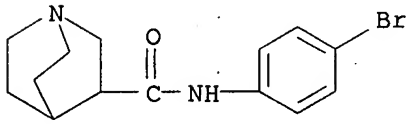


RN 604803-85-2 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(4-bromophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RN 604804-18-4 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(4-bromophenyl)- (CA INDEX NAME)

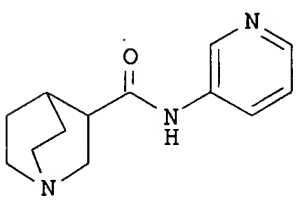


REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:506550 CAPLUS
DOCUMENT NUMBER: 139:85529
TITLE: Preparation of monocyclic N-aryl amides for improvement of the perception and memory enhancement
INVENTOR(S): Luithle, Joachim; Boess, Frank-Gerhard; Erb, Christina; Flessner, Timo; Hendrix, Martin; Van Kampen, Marja; Methfessel, Christoph
PATENT ASSIGNEE(S): Bayer AG, Germany
SOURCE: Ger. Offen., 10 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10162442	A1	20030703	DE 2001-10162442	20011219
PRIORITY APPLN. INFO.:			DE 2001-10162442	20011219

OTHER SOURCE(S): MARPAT 139:85529
GI



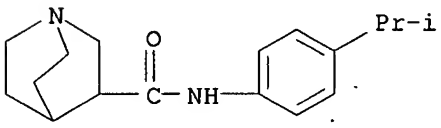
I

AB The invention concerns the use of monocyclic N-aryl amides, R1CONR2R3 [R1 = 1-azabicyclo[m.n.p]alkyl (7 - 11 ring atoms, optionally substituted with C1-6-alkyl); m, n = 2 , 3; p = 1 - 3; R2 = (un)substituted Ph, 5 to 6-membered heteroaryl (optionally substituted with halogen, CHO, CONH2, CN, CF3,CF3O, NO2, C1-6-alkyl, C1-6-alkoxy, C1-6-alkylthio); R3 = H, C1-6-alkyl] and their salts, solvates and solvate salts, in the production of drugs for the improvement of the perception, concentration achievement, learning achievement and/or memory achievement as well as to new monocyclic N-aryl amides. Thus, N-(3-pyridinyl)quinuclidine-3-carboxamide dihydrochloride (I·2HCl) was prepared from quinuclidine-3-carboxylic acid chloride hydrochloride and 3-aminopyridine in DMF containing EtN(CHMe2)2 and catalytic DMAP. The affinity of I for α7-nAChR was determined (no data).

IT 552832-93-6P, N-(4-Isopropylphenyl)quinuclidine-3-carboxamide hydrochloride
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of monocyclic N-aryl amides for improvement of the perception and memory enhancement)

RN 552832-93-6 CAPLUS

CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4-(1-methylethyl)phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L4 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1991:199358 CAPLUS

DOCUMENT NUMBER: 114:199358

TITLE: EO-199, a specific antagonist of antiarrhythmic drugs: assessment by binding experiments and in vivo studies

AUTHOR(S): Oppenheimer, Edna; Harel, Gideon; Lipinsky, Dafna; Sarne, Yosef

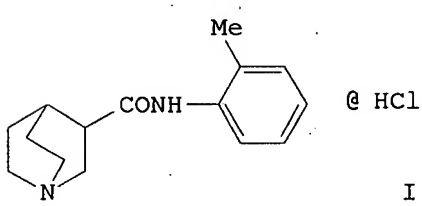
CORPORATE SOURCE: Sackler Fac. Med., Tel-Aviv Univ., Ramat-Aviv, 69978, Israel

SOURCE: Life Sciences (1991), 48(10), 977-85
CODEN: LIFSAK; ISSN: 0024-3205

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



@ HCl

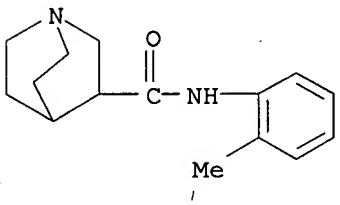
I

AB EO-199 (I), a demethylated analog of the novel class I antiarrhythmic drug EO-122, was found to antagonize the antiarrhythmic activity of EO-122 and that of procainamide (Class I). EO-199 did not block the activity of a class IB antiarrhythmic agent, lidocaine. EO-199 also displaced the specific binding of [3H]EO-122 to rat heart membranes similarly to procainamide, whereas lidocaine did not. The correlation between binding expts. and pharmacol. effects points to a possible subclassification of these drugs. The 2 chemical analogs EO-199 and EO-122, as well as procainamide (IA) but not lidocaine (IB), compete at the same site or the same state of the sodium channel. The availability of a specific antagonist might be useful for studying the mechanism of action of antiarrhythmic drugs as well as an antidote in cases of antiarrhythmics overdose intoxication.

IT 133658-30-7, EO 199
RL: BIOL (Biological study)
(antiarrhythmic agents antagonism by, poisoning by antiarrhythmics in relation to)

RN 133658-30-7 CAPLUS

CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(2-methylphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L4 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1990:69427 CAPLUS

DOCUMENT NUMBER: 112:69427

TITLE: Molecular modeling studies on class Ia and Ib antiarrhythmics. Model representations for differentiating binding sites

AUTHOR(S): Marrer, S.

CORPORATE SOURCE: Pharm. Inst., Freie Univ. Berlin, Berlin, Fed. Rep. Ger.

SOURCE: Pharmaceutica Acta Helvetiae (1989), 64(12), 338-44
CODEN: PAHEAA; ISSN: 0031-6865

DOCUMENT TYPE: Journal

LANGUAGE: German

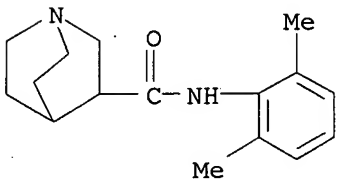
AB The mol. properties of quinidine, EO 122, and lidocaine were investigated using theor. mol. modeling. The binding patterns of the mols. were investigated by calculating interaction energies with a neg. charged fragment (receptor model). Based on these calcns. a model for the differentiation of class Ia and class Ib antiarrhythmic drugs could be deduced. The results fit the modulated receptor hypothesis. The mol. basis for the preferred affinity of quinidine to the open state of the sodium channel and the equal affinity of lidocaine to the open and inactivated state of the channel were defined.

IT 23581-62-6, EO-122
RL: BIOL (Biological study)
(mol. modeling of heart sodium channel receptor interaction with)

RN 23581-62-6 CAPLUS

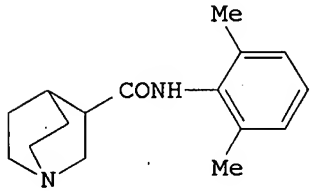
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(2,6-dimethylphenyl)-,

monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L4 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:400428 CAPLUS
DOCUMENT NUMBER: 111:428
TITLE: The specific binding of [3H]EO-122, a radiolabeled class I antiarrhythmic drug, to rat heart membranes
AUTHOR(S): Oppenheimer, Edna; Meiri, Hamutal; Ori, Yaacov
CORPORATE SOURCE: Sackler Fac. Med., Tel Aviv Univ., Ramat Aviv, 69978, Israel
SOURCE: Journal of Molecular and Cellular Cardiology (1989), 21(2), 223-30
CODEN: JMCDAY; ISSN: 0022-2828
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



@ HCl

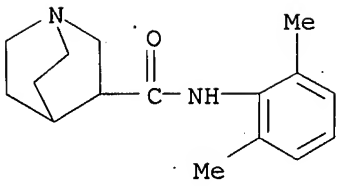
I

AB [3H]EO-122 (I), a radiolabeled class I antiarrhythmic drug, was used to characterize a new specific binding system to rat heart membranes. The binding was saturable and competitive with unlabeled EO-122 and other antiarrhythmic drugs. In this system, [3H]EO-122 bound to 2 sites: site A with an apparent Kd of 33.5 nM, Bmax of 1.05 pmol/mg protein and Hill coefficient nH = 4 and site B with an apparent Kd of 233 nM, Bmax of 5.7 pmol/mg protein and nH = 6. The binding to site B indicates that this site is pharmacol. relevant to known class IA antiarrhythmic drugs such as quinidine and procainamide. Lidocaine (class IB) did not interact with this site. Interpretation of the high Hill coefficient suggests that the binding of an antiarrhythmic drug to its pharmacol. relevant binding site exposes addnl. binding sites and/or modulates the affinity of adjacent binding sites.

IT 23581-62-6, EO 122
RL: PROC (Process)
(binding of, by heart membrane)

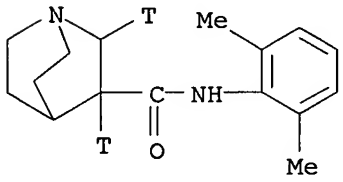
RN 23581-62-6 CAPLUS

CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(2,6-dimethylphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



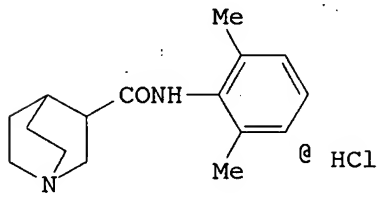
● HCl

IT 120949-68-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and binding by heart membrane of)
RN 120949-68-0 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-2,3-t2-3-carboxamide, N-(2,6-dimethylphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L4 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:611641 CAPLUS
DOCUMENT NUMBER: 107:211641
TITLE: Electrophysiological effects of a novel antiarrhythmic drug, EO-122, on guinea pig ventricular muscle and isolated myocytes
AUTHOR(S): Binah, Ofer; Gilat, Eran; Rubinstein, Irit; Oppenheimer, Edna
CORPORATE SOURCE: Rappaport Family Inst. Res. Med. Sci., Fac. Med., Haifa, 31096, Israel
SOURCE: Journal of Cardiovascular Pharmacology (1987), 10(3), 301-8
CODEN: JCPCDT; ISSN: 0160-2446
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

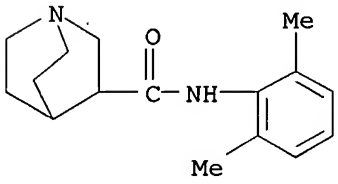
AB The effects of EO-122 (I) on the electrophysiol. properties of guinea pig papillary muscle and ventricular myocytes were investigated by means of

standard microelectrode and whole-cell recording techniques, resp. At the concentration range of 10-7-10-4 M (cycle length, 2000 ms), resting potential and
action potential duration (APD90) were not altered by the drug. Action potential amplitude and APD50 were reduced by 10-4 M, and Vmax was reduced by EO-122 ≥10-5 M. The effect of EO-122 on Vmax was use-dependent. At 10-6 and 10-5 M (cycle length, 2000 ms), the time constant for onset of block (τon) was 37.0 and 26.0 s, resp. The recovery kinetics from use-dependent block was not monoexponential, and the estimated "time constant" for recovery was 76.5 s. The effects of EO-122, 10-5 M on the membrane currents in ventricular myocytes were examined and it was found that the drug attenuated the slow inward current (Isi). The present study demonstrates that EO-122 blocks both the fast inward (Na+) and the slow inward (Ca2+) channels, and these effects are probably responsible for the antiarrhythmic effects of the drug.

IT 23581-62-6, EO-122
RL: BIOL (Biological study)
(heart elec. activity response to, antiarrhythmic mechanism in relation to)

RN 23581-62-6 CAPLUS

CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(2,6-dimethylphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L4 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1981:424851 CAPLUS
DOCUMENT NUMBER: 95:24851
TITLE: Process for the preparation of quinuclidine carboxylic acid derivatives
PATENT ASSIGNEE(S): Mundipharma A.-G., Switz.
SOURCE: Brit., 3 pp. Division of Brit. 1,578,421.
CODEN: BRXXAA
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 1578422	A	19801105	GB 1979-21014	19780119
IL 51296	A	19831031	IL 1977-51296	19770119
GB 1578421	A	19801105	GB 1978-2197	19780119
PRIORITY APPLN. INFO.:			IL 1977-51296 A	19770119
			GB 1978-2197	19780119

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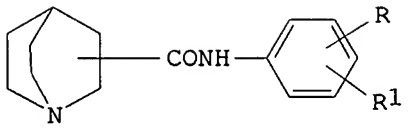
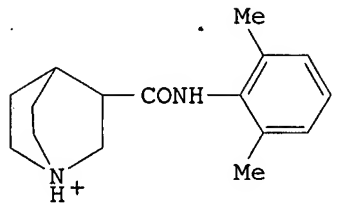


I

II



Cl^-

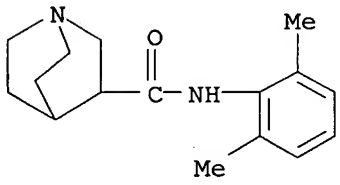
III

AB The title compds. I (R, R1 = H, halo, C1-6 alkyl) were prepared by treating a quinuclidinecarboxylate II or its acid addition salts with H2NC6H3RR1 (R, R1 as before) in anhydrous alc.-free CHCl3 containing (COCl)2. E.g., 2.5 g of the HCl addition salt of II (CO2H group in 3-position) was refluxed 3 h in 150 mL anhydrous alc.-free CHCl3 containing 10 mL (COCl)2, then treated with 3 g H2NC6H3Me2-2,6 in 100 mL CHCl3 (reflux, 6 h) to give, after work-up, 3 g (91%) III. III has useful antiarrhythmic properties (no data).

IT 23581-62-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, of, as antiarrhythmic)

RN 23581-62-6 CAPLUS

CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(2,6-dimethylphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L4 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1980:561251 CAPLUS

DOCUMENT NUMBER: 93:161251

TITLE: A preclinical study of EO-122, a new lidocaine-like antiarrhythmic drug

AUTHOR(S): Oppenheimer, Edna; Kaplinsky, Eliezer; Kariv, Naam; Bruckstein, Rachel; Cohen, Sasson

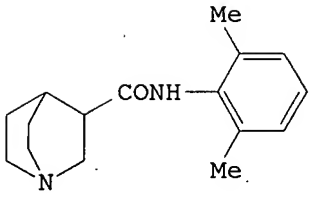
CORPORATE SOURCE: Sackler Sch. Med., Tel-Aviv Univ., Kfar Saba, Israel

SOURCE: Angiology (1980), 31(6), 410-26
CODEN: ANGIAB; ISSN: 0003-3197

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



@ HCl

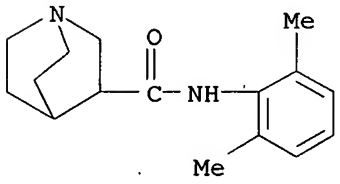
I

AB Restoration of normal sinus rhythm and suppression of ouabain-induced arrhythmia in cats and dogs, and of coronary occlusion-induced arrhythmia in dogs, followed a single i.v. injection of 1-3 mg EO 122 (I) [23581-62-6]/kg, with an onset of 2 min and a duration of 20-240 min. Occlusion-induced arrhythmia was also suppressed after an oral dose of 10-20 mg/kg, with an onset of 11-65 min and a duration of 25-120 min. Under similar conditions, lidocaine was either totally ineffective or of ultra-short duration. The bioavailability of EO-122 by the oral route exceeded 80% of the oral dose. Therapeutic blood concns. were in the range 0.5-7 μg/mL. At about 5 μg/mL, there was a slight depression of cardiac function in the anesthetized cat, but not in the conscious dog. In cats, complete A-V block occurred at concns. of 60-70 μg/mL. The i.v. LD50 in mice was 22 mg/kg and in rabbits 8.5 mg/kg. No overt signs of neurotoxicity could be observed at any dose of EO-122. The pharmacokinetic profile of the drug fits a two-compartment open model, with t1/2 .simeq.150 min.

IT 23581-62-6
RL: BIOL (Biological study)
(heart arrhythmia response to)

RN 23581-62-6 CAPLUS

CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(2,6-dimethylphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L4 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1979:92467 CAPLUS

DOCUMENT NUMBER: 90:92467

TITLE: Solvent-caused quaternization as a possible source of error in the mass spectral quantitation of tertiary amines. I. Methylene chloride quaternization

AUTHOR(S): Vincze, Adam; Gefen, Leon

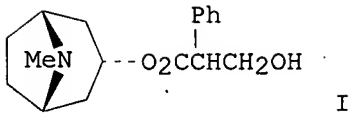
CORPORATE SOURCE: Israel Inst. Biol. Res., Ness Ziona, Israel

SOURCE: Israel Journal of Chemistry (1978), 17(3), 236-8
CODEN: ISJCAT; ISSN: 0021-2148

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



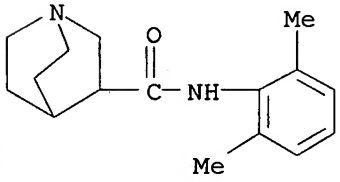
I

AB Basic tertiary amines such as atropine (I) [51-55-8] and derivs. of N-methylpiperidine and quinuclidine, tend to quaternize in CH2Cl2 [75-09-2] at room temperature The quaternary ammonium salts formed undergo various dequaternization reactions in the heated direct inlet probe of the mass spectrometer, giving rise to volatile tertiary amines that are different from the starting material and usually having higher mol. wts. Recorded spectra of such samples are a superposition of those of the various tertiary amines constituting the mixture If just a few relevant and abundant ions in the mass spectrum of the original tertiary amine are monitored, as in quant. fragmentog. rather low results might be obtained. Moreover, the operator may be quite unaware of the fact that only part of the sample is being measured.

IT 69267-68-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(methylene chloride quaternization of, mass spectroscopic error in relation to)

RN 69267-68-1 CAPLUS

CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(2,6-dimethylphenyl)- (9CI) (CA INDEX NAME)



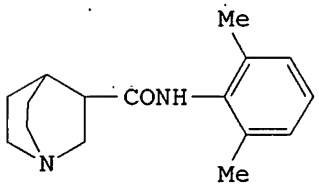
L4 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1978:546786 CAPLUS
DOCUMENT NUMBER: 89:146786
TITLE: Antiarrhythmic quinuclidine carboxylic acid xylidide
INVENTOR(S): Oppenheimer, Edna; Kaplinsky, Eliezer; Cohen, Sasson
PATENT ASSIGNEE(S): Mundipharma A.-G., Switz.
SOURCE: Ger. Offen., 24 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2802208	A1	19780720	DE 1978-2802208	19780119
IL 51296	A	19831031	IL 1977-51296	19770119
ZA 7707476	A	19781025	ZA 1977-7476	19771215
FI 7703923	A	19780720	FI 1977-3923	19771223
ES 465827	A1	19790101	ES 1978-465827	19780107
SE 7800204	A	19780720	SE 1978-204	19780109
SE 443786	B	19860310		
SE 443786	C	19860619		
AU 7832489	A	19790726	AU 1978-32489	19780117
AU 519089	B2	19811105		
DK 7800264	A	19780720	DK 1978-264	19780118

DK 147180	B	19840507			
DK 147180	C	19841112			
NO 7800177	A	19780720	NO 1978-177		19780118
NO 148335	B	19830613			
NO 148335	C	19830921			
FR 2384499	A1	19781020	FR 1978-1354		19780118
FR 2384499	B1	19811030			
AT 7800353	A	19790815	AT 1978-353		19780118
AT 355586	B	19800310			
CA 1107734	A1	19810825	CA 1978-295163		19780118
JP 53109952	A	19780926	JP 1978-4764		19780119
JP 63008111	B	19880219			

PRIORITY APPLN. INFO.: IL 1977-51296 A 19770119
OTHER SOURCE(S): MARPAT 89:146786
GI



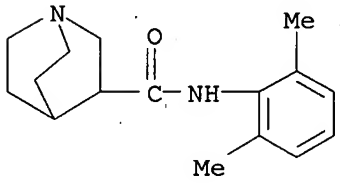
I

AB The title compound (I) was prepared in 91% yield by treating 3-quinuclidinecarboxylic acid-HCl with oxalyl chloride and 2,6-Me2C6H3NH2. I has superior antiarrhythmic activity to lidocaine. The 2-quinuclidine analog of I is inactive and neurotoxic.

IT 23581-62-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antiarrhythmic activity of)

RN 23581-62-6 CAPLUS

CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(2,6-dimethylphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

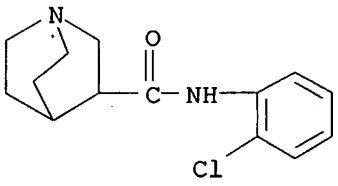
L4 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1970:78905 CAPLUS
DOCUMENT NUMBER:	72:78905
ORIGINAL REFERENCE NO.:	72:14365a,14368a
TITLE:	2(and 3)-Quinuclidine carboxanilides
INVENTOR(S):	Sandberg, Rune V.; Sjoberg, Berndt O. H.; Tegner, Claes P.
PATENT ASSIGNEE(S):	Aktiebolag Astra

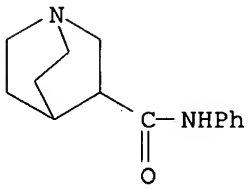
SOURCE: Fr., 7 pp.
CODEN: FRXXAK
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 1566045		19690502	FR	19680522
DE 1770414			DE	
FR 7713			FR	
GB 1176757			GB	
SE 331841			SE	
US 3579523		19710518	US	19680517
US 3726980		19730410	US	19701026

PRIORITY APPLN. INFO.: SE 19670523
OTHER SOURCE(S): MARPAT 72:78905
GI For diagram(s), see printed CA Issue.
AB The title compds. (I) and (II), which have antiarrhythmic and local anesthetic effects, were prepared from derivs. of quinuclidine-2(or 3)-carboxylic acids (Renk, E.; et al., 1954). Thus, a mixture of 4.5 g Me quinuclidine-2-carboxylate, 2.9 g o-toluidine, and 0.1 g Na was kept 5 hr at 140° and worked up to give 2.1 g I (R1 = H, R2 = Me), m. 115.5-17° (aqueous EtOH). Similarly prepared were the following I (R1, R2, and m.p. HCl salt given): H, Cl, - [base m. 117-19.5° (aqueous EtOH)]; Me, Me, 223-5° (EtOH-isoPr2O); Me, Et, 209-11° (MeCOPr); Et, Et, 209.5-11.5° (MeCN). Also prepared were II (R = Cl), m. 166.5-8.5° (MeCOBu-iso), and II (R = H), m. 178-80° (MeCOBu-iso).
IT 26801-43-4P 26801-44-5P
RL: SPN (Synthetic preparation); PREP (Preparation).
(preparation of)
RN 26801-43-4 CAPLUS
CN 3-Quinuclidinecarboxanilide, 2'-chloro- (8CI) (CA INDEX NAME)



RN 26801-44-5 CAPLUS
CN 3-Quinuclidinecarboxanilide (8CI) (CA INDEX NAME)



L4 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1969:461176 CAPLUS
DOCUMENT NUMBER: 71:61176
ORIGINAL REFERENCE NO.: 71:11251a,11254a

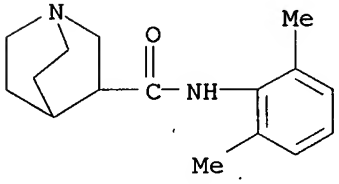
TITLE: Some derivatives of quinuclidine-3-carboxylic acids
AUTHOR(S): Dahlbom, Richard; Dolby, Jorgen
CORPORATE SOURCE: Farm. Fak. Stockholm, Stockholm, Swed.
SOURCE: Acta Pharmaceutica Suecica (1969), 6(2), 277-82
CODEN: APSXAS; ISSN: 0001-6675
DOCUMENT TYPE: Journal
LANGUAGE: English

GI For diagram(s), see printed CA Issue.

AB Me dehydroquinuclidine-3-carboxylate-HCl (Ia.HCl) (2.4 g.) in 20 ml. 33% aqueous MeNH2 was kept 48 hrs. at room temperature, and worked up to give 54% I (R = NHMe), m. 201-2°. Other amides similarly prepared were as follows [compound type, R (or R and R1), % yield, salt, and m.p. salt given]: II, NHMe, H, 47, HCl, 229-30°; II, NHEt, H, 40, HCl, 270-1°; I, NHEt, 63, oxalate, 169-72°; I, NHPr, 69, oxalate, 112-15°; and I, NHBu, 71, oxalate, 98-102°. Me quinuclidine-3-carboxylate-HCl (2.1 g.) in 20 ml. 20% HCl was refluxed 15 hrs., dried, 15 ml. SOCl2 added, the mixture refluxed 3 hrs. and dried, 2.4 g. 2,6-Me2C6H3NH2 was added dropwise, 2.7 g. K2CO3 and 20 ml. CHCl3 were added, and the mixture refluxed 3 hrs. and worked up to give 60% II.HCl (R = 2,6-Me2C6H3NH, R1 = H), m. 236-8°. The following compds. were similarly prepared [compound type, R (or R and R1), % yield, salt, and m.p. salt given]: II, pyrrolidine, H, 48,-(free base), 99-100°; I, NMe2, 54, HCl, 180-2°; I, NEt2, 32, HCl, 168-70°; I, pyrrolidino, 39,-(free base), 87-8.5°; I, piperidino, 36, HCl, 183-4°; II, 2-MeC6H4NH, H, 55,-(free base), 169-70°; II, 2,6-MeClC6H3NH, H, 52, HCl, 226-8°; I, 2-MeC6H4NH, 49, HCl, 208-9°; I, 2,6-Me2C6H3NH, 45, HCl, 247-8°; and II, 2,6-MeClC6H3NH, 52, HCl, 236-7°. Ia was added to a solution of Na in the appropriate amino alc., and the mixture heated 6 hrs. at 70°/100 mm. to give the following II (R, R1, % yield, and m.p. given): O(CH2)2NMe2, OH, 73, 103-5°; O(CH2)2NEt2, OH, 73, 73-4.5°; pyrrolidinoethoxy, OH, 79, 90-1.5°; and piperidinoethoxy, OH, 82, 100-2°. III were prepared by treating the appropriate amino esters in Me2CO with MeI. The salt separated almost immediately and was collected and recrystd. from 90% EtOH. The following III were prepared (R, % yield, and m.p. given): NMe3, 95, 239-40°; NMeEt2, 92, 249-50°; N-methylpyrrolidino, 95, 247-8°; and N-methylpiperidino, 89, 248-9°. All the compds. were tested for pharmacol. and microbiol. activities, but showed no appreciable effects.

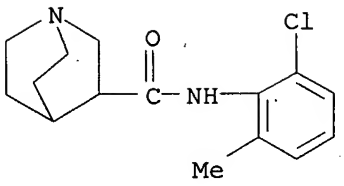
IT 23581-62-6P 23581-63-7P 23692-14-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 23581-62-6 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(2,6-dimethylphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



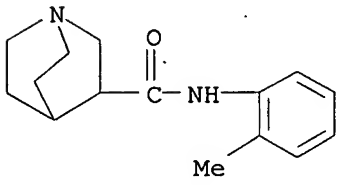
● HCl

RN 23581-63-7 CAPLUS
CN 3-Quinuclidinecarboxy-o-toluidide, 6'-chloro-, monohydrochloride (8CI) (CA INDEX NAME)



● HCl

RN 23692-14-0 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(2-methylphenyl)- (9CI) (CA INDEX NAME)



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FULL ESTIMATED COST	74.72	247.03
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CA SUBSCRIBER PRICE	-10.92	-10.92

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EAST Search History

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L2	78	l1 and quinuclidin	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2007/10/17 17:04
L3	1	l2 and acetylcholin	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2007/10/17 17:04
L4	26	l2 and nicotinic	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2007/10/17 17:04